

The University of Chicago

STUDIES ON THE HISTOPATHOLOGY OF
THE PALATINE TONSILS AND ON THE
IMMUNOLOGICAL REACTIONS OF
THE ADJACENT TISSUES

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
BIOLOGICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF PATHOLOGY

1932

By

ROBERT STEWART JASON

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PART I
PATHOLOGIC CHANGES IN THE HUMAN
PALATINE TONSIL
Their Correlation with the Clinical
Findings

The pathologic changes which occur in human palatine tonsils as a result of local infection are well known, for they have been studied extensively in many laboratories, and tabulations and descriptions of these changes have appeared in the literature (Welch, 1; Nelson, 2). It is also known that when a large number of the tonsils removed as a routine are studied in the laboratory, a relatively large percentage are found to be normal. On the other hand, Kellert (3) found that the tonsillar changes in the clinically healthy young adult are similar in character though less extensive than those in patients with chronic local disease, and he failed to find distinctive changes due to the hemolytic streptococcus. It is not surprising, therefore, that studies on the correlation of the clinical and the laboratory data on the tonsils have not given encouraging results. For instance, Turley (4) attempted to correlate the bacteriologic, pathologic and clinical data in tonsillar disease and concluded that "no definite connections can be shown between" them, and Lippincott (5), who made a similar study, was led to report that "there are no bacteriological or morphological findings typical of any given symptom or complaint."

Most of the studies in which the pathologic changes in the tonsils have been taken into consideration have been based on observations on one or two sections made in the course of the routine study of a large amount of surgical material. In the light of the present understanding of the function of the reticulo-endothelial system, and the pluri-potentiality of the lymphocyte as proved by Maximow and Bloom (6), it seems reasonable to assume that a closer study of the cellular components of the tonsil, with a large number of sections from each specimen, may yield information of value. In Maximow's study of inflammation, he observed that cells in the stages of transition from lymphocytes to

monocytes and thence to fibroblasts were most abundant and most easily identified in acute inflammation. As human tonsillar material is obtained, in the majority of cases, from patients in whom the local acute inflammation has subsided and the tissues have returned to a state approaching the "physiologic conditions," it is difficult to find and to identify cells in the stages of transition from lymphocytes to macrophages. Yet, the healing or healed stages of the inflammatory process are visible, so that it should be possible to find cells approaching or in the fibroblastic stage, and these changes should appear where the infection is greatest, i.e., about the crypts. Further, the type of correlation which has been sought between the clinical and the laboratory data in tonsillar disease has been a correlation of specific clinical findings with specific pathologic or bacteriologic changes, that is, a qualitative rather than a quantitative correlation. Kellert's observation that in the healthy young adult the pathologic changes are similar to, though not so extensive as, those found in patients with chronic local disease suggests that there may possibly be some quantitative correlation between the pathologic and the clinical data. As it seemed advisable to test the validity of these assumptions, a study of the pathologic changes in the human palatine tonsil was undertaken, and the data were correlated with the clinical indications for tonsillectomy.

MATERIAL AND PROCEDURES

Tonsils were obtained from thirty-five consecutive tonsillectomies performed at the Billings Hospital, and from five patients operated on in one day at the Children's Memorial Hospital. Twenty-four of the patients were males and sixteen, females; they ranged in age from the first to the sixth decade. In six patients, from 7 to 45 years of age, the removed tonsils were "recurrences." Acute nasopharyngeal disease was not present in any patient at the time of operation.

The diameter of each tonsil was determined by measurement, and the volume, by the amount of fixing fluid displaced above the 50 cc. level in a 100 cc. graduate. Fractions of a cubic centimeter were measured with a vernier caliper. All tissues were fixed in formaldehyde-Zenker fluid, embedded in pyroxylin (celloidin) and bisected longitudinally in a plane perpendicular to the surface covered by epithelium. From the central portion of

each tonsil fifty sections were cut at 15 microns; they were mounted in series and stained with Maximow's hematoxylin-eosin-azur II. Serial sections for macroscopic examination were made from the remainder of each tonsil with a sharp razor.

RESULTS

The relationship of the age of the patients to the degree of tonsillar enlargement appears in Table I. The histopathologic changes in this series correspond, in general, with those found by Kellert in the clinically normal young adult and with those obtained by Welch and Nelson in patients. Though lymphocytes and, less frequently, plasma cells were found in the crypts and infiltrating the epithelium, trabeculae and capsule and, on occasions, the tissues adjacent to the tonsils, only a few mononuclear cells of somewhat larger size and suggestive of transitions from lymphocytes to large phagocytic cells were seen in these sites. Tissue repair appeared to take place as an encroachment on the lymphoid elements by granulation tissue or adult connective tissue, depending on the age of the lesion, either from the marginal subepithelial connective tissue or from the capsule and the trabeculae. Tumors, abscesses or large ulcerations in the crypts, acute inflammation or peritonsillar abscesses were not found. Some degree of correlation between the clinical findings and the pathologic changes is shown in Table II.

COMMENT

If the average longitudinal diameter of the tonsil is considered to be from 2.3 to 2.5 cm. (Kellert, 3; Turley, 4), in this series the tonsils of the patients in the age period from 26 to 35, inclusive, were above the average size and the tonsils of those in the remaining age groups were of average, or below the average, size. Similarly, when the size of the tonsils was determined by volume (Table I), the tonsils of patients in the first decade showed a much greater average enlargement than those of patients in the second decade, but the greatest enlargement occurred in the third and fourth decades, with a gradual decrease in size through the fifth and sixth decades. The observations in this small series correspond, in a general way, with those of Blos (7), Schönberger (8) and Pirquet (9), who studied a large number of cases. As almost all of the patients in this series

TABLE I

NUMBER OF PATIENTS IN THE VARIOUS AGE GROUPS AND THE AVERAGE SIZE OF THEIR TONSILS

Age of patients	1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60
Number of patients*....	1	2	1	2	10	6	3	3	3	2	2	0
Number of patients.....	3		3		16		6		5		2	
Average size of tonsils, cc.	4.08		2.85		5.28		4.15		3.11		2.53	
Average size of "recurrent" tonsils.....	Children (1) 0.16						Adults (5) 3.48					

*The ages of the five patients from the Children's Memorial Hospital were not obtained.

TABLE II

RELATIONSHIP OF PATHOLOGIC CHANGES TO CLINICAL CAUSES FOR TONSILLECTOMY*

	Reasons for Removal of Tonsils		
	Group 1 Local Reasons (15 Patients)	Group 2 Focal Reasons (10 Patients)	Group 3 Local and Focal Reasons (12 Patients)
Tonsils enlarged above average.....	40.0	50.0	8.3
Crypts:			
Invasion of epithelium.....	73.3	90.0	66.7
Polymorphonuclears.....	73.3	90.0	50.0
Ulcers.....	6.7	20.0	41.7
Capsule scars.....	33.3	80.0	83.3
Trabecular scars.....	66.7	90.0	75.0
Cartilage.....	13.3	20.0	58.3
Bone.....	6.0	10.0	41.6
Lymphoid hyperplasia:			
None.....	0.0	10.0	16.7
Slight.....	20.0	70.0	58.3
Moderate.....	100.0	70.0	66.7
Marked.....	13.3	10.0	8.3
Diffuse scarring.....	13.3	90.0	66.7

*Recorded in per cent of patients.

were adults, the physiologic enlargements noted by Pirquet do not appear, except for the relatively larger tonsils found in persons in the first decade as compared with those in the second decade, but the pathologic enlargement he described in adults does occur.

The pathologic change labeled "invasion of epithelium" in Table II consisted of granulation tissue-like changes in which capillaries could be seen extending into the epithelial zone, the boundaries of which had become obscured by round cell infiltration and by an irregular down-growth of epithelial cells, with an apparent loss of basement membrane. The first impression produced by such areas is that with blood vessels so near the lumen of crypts laden with bacteria it should be easy for organisms to gain access to the systemic circulation. On the other hand, the close resemblance of this pathologic change to granulation tissue suggests that possibly here, as in the granulation tissue of wounds healing by second intention, the resistance to the invasion of bacteria is great and the danger of systemic infection, therefore, relatively slight. This appears to be supported by the fact that in Table II this type of pathologic change shows a relatively high incidence whether the patient's tonsils were removed for local, focal or both local and focal reasons.

The tonsils used in this study were obtained from patients in whom there was no acute inflammation of the throat, which accounts for the small number of cells seen in transition stages from lymphocytes to macrophages. It follows, therefore, that the observations made here do not invalidate the opinion that the tonsil may be an organ of defense in which potential phagocytes, as it were, are stored, but it is difficult to understand why the repair of the tonsil appeared as a growth of the perivascular connective tissue from the capsule, trabeculae or marginal sub-epithelial connective tissue and not as a focal transformation about the crypts.

CORRELATION

As attempts to correlate single pathologic changes with single clinical findings are so unsatisfactory, it seemed desirable to see whether a quantitative correlation between the pathologic and the clinical data could be established. Accordingly, the patients in this study were arranged in three groups on the basis of their clinical histories and physical findings as

follows: group 1, fifteen patients whose tonsils were removed for local reasons alone; group 2, ten patients whose tonsils were removed in an effort to eradicate foci of infection, and group 3, twelve patients whose tonsils were removed for both local and focal reasons. Three patients could not be classified in this way because their charts did not include sufficient data to indicate whether there were local, focal or both local and focal reasons for tonsillectomy. A list was made of the types of pathologic change which were considered to be adequate indications of local reaction or damage, and the percentage of the patients showing these types of pathologic change was determined for each group. The data obtained are shown in Table II. It is apparent at a glance that there is some striking correlation between the incidence of certain types of change and the three groups of patients listed. Experiments on the vital staining of the human tonsil by Wassilieff (10) show that dyes injected into the tonsil are spread first throughout the connective tissue stroma, and that fibrosis favors, whereas hyperplasia of the lymphoid tissues reduces, the speed of spreading. If this is true where bacteria are concerned, it is significant that in groups 2 and 3 the types of pathologic change most frequently found were those which would favor the entrance of bacteria from the crypts into the systemic circulation, whereas in group 1 hyperplasia of the lymphoid elements of the tonsil was the most striking feature.

In connection with the debate of long standing on the origin of the cartilage and bone found in the tonsils, it is interesting to note the increasing incidence of these structures from group 1 to group 3. It is of interest also to note the frequency of infection of the upper respiratory tract and enlargement of the cervical lymph nodes in these groups: In group 1, 95.5 and 60 per cent of the patients had infections of the upper respiratory tract and cervical lymphadenopathy, respectively; in group 2, the percentages were 40 and 10, respectively, and in group 3, 66.7 and 33.3. This lower incidence of infection of the upper respiratory tract and enlargement of the cervical lymph nodes in the last two groups is in accord with the clinical observation that it is frequently the small, silent and buried tonsil, rather than the large and obviously inflamed one, which is most to be feared as a focal infection from which disease elsewhere in the body may arise.

CONCLUSIONS

Though this series is too small to serve as a basis for conclusions, it is suggestive along the following lines:

1. In the human palatine tonsils removed as a routine there is little evidence of the transformation of lymphocytes into macrophages.
2. Repair in tonsillar disease occurs as an ingrowth of granulation tissue from the capsule, trabeculae or marginal sub-epithelial connective tissue and not by the focal transformation of lymphocytes about the crypts.
3. In general, the patients with local complaints and physical signs of tonsillar disease have relatively fewer pathologic changes in their tonsils than those with systemic disease or disease elsewhere in the body attributable to the tonsils.
4. Young adults may show as marked tonsillar enlargement as children, in whom enlarged lymphoid structures are common.

PART II
LOCAL TISSUE IMMUNITY OF THE TONSILLAR REGION
OF THE RABBIT

Animal and biochemical experiments (Schmidt, 11; Russ, Suchanek, and Pichler, 12; and Luscher, 13) carried out within the last fifteen years with tonsillar extracts and studies of cultures of tonsil tissues (Kelemen, 14; Kelemen and Hassako, 15), probably have contributed more toward the solution of the "tonsil problem" than all of the earlier work on human material alone, yet these too indicate that further experimentation and other methods of approach are necessary to answer fully the "tonsil question." A new method of approach to this problem is suggested by the recent contributions on local tissue immunity.

The phenomenon of local tissue immunity, in contradistinction to systemic immunity, was given new emphasis by Besredka (16) and was more fully explained by Gay (17) and his collaborators, who emphasized the importance of local collections of macrophages in the disposal of offending organisms. Cannon and Pacheco (18) observed that the production of active local immunity of the skin of the guinea-pig by intracutaneous injections of staphylococcus vaccines, was attended by a marked thickening of the subreticular layer of the subcutis, due mainly to the fact that the immunized site had become crowded with macrophages. In the subsequent demonstration of local immunity, these cells were concerned with the ultimate disposal of the live and virulent staphylococci, and their presence was associated with an *in vivo* agglutination-like reaction of the specific organisms. Their experiments suggested that these cells were derived from the vascular mononuclear cells and from specialized local tissue cells, which is in accord with the experimental results of Maximow and Bloom (6), who traced the development of macrophages from vascular lymphocytes and observed the transformation of tissue "resting wandering cells" into phagocytic cells.

The experimental demonstration of the facts that macrophages play a very important part in local tissue immunity and that lymphocytes and certain tissue cells are potential macro-

phages, lends weight to the theory that in the tonsil Nature has probably evolved an organ of defence of maximum potential strength for the amount of space occupied (Lectures, 19). I believe that this theory has not been tested experimentally but there is some clinical evidence in its favor. Digby (20) referred significantly to the oral immunization against bacillary dysentery and Malta fever by Nicolle and Conseil; against typhoid fever by Vaillant, and to Dudley's demonstration that exposure to diphtheritic infection without contracting the disease clinically, leads to immunity as shown by the Schick test. He believed that this immunity was effected through the subepithelial lymphoid nodules of the digestive tract, of which the tonsil is the largest. Bloomfield and Felty (21) found that the carriage of beta-hemolytic streptococci in the tonsils seemed to prevent attacks of acute tonsillitis and that "the resistance was directly related to the continued presence of the streptococcus in the carrier" for "a high degree of susceptibility was readily re-established after the carrier state was terminated." Zingher (22) reported the development of diphtheria in carriers following tonsillectomy. In his cases, though there was no systemic immunity against diphtheria, the disease had been held in check effectively by the local immunity or resistance of the tonsillar tissues until this was destroyed by tonsillectomy.

On the other hand, the theory that the tonsil is an organ of defence is not supported by many of the studies based on a comparison of the clinical histories of large numbers of tonsillectomized and non-tonsillectomized children and adults (Kaiser, 23; Cunningham, 24) and it is difficult to explain the association which is found frequently of infected tonsils with systemic disease or localized disease elsewhere in the body, without an obvious portal of entrance of micro-organisms except the tonsils. Yet, in the evaluation of these studies one is impressed by the following facts: First. It is a difficult matter to establish the borderline between diseased and healthy tonsils. The frankly infected tonsil is recognized readily enough in the laboratory if not in the clinic. Most tonsils, however, are removed after the subsidence of acute local symptoms and it is then very difficult, in a given case, to determine how harmful the remaining, slightly evident, infection may be and to what extent the hyperplasia of the tonsil may have been and still is effective in holding in

check the infection lurking in the tonsil crypts. Second. There is not a close correlation between clinical symptoms and the pathological changes found in the tonsils removed routinely, so that many individuals in good health are found to have moderately or heavily infected tonsils. Third. It is not practicable to measure the degree of local immunity which a tonsil has prior to its removal.

The very nature of these difficulties encountered clinically suggests that perhaps they can be studied more effectively by means of animal experimentation, using, possibly, some of the methods employed in the study of local tissue immunity. Thus, it should be possible: to immunize actively the tonsils or the tonsillar region; to determine whether this local immunity is associated with hyperplasia of the tonsil or not; to measure this immunity by comparing it with that produced in a similar way elsewhere in the oral cavity, and to see to what extent the tonsillar lymphocytes are mobilized and converted into macrophages.

MATERIALS AND PROCEDURES

Thirty-six rabbits were used, divided into two groups of ten and one of sixteen, which are herein designated as Groups A, B and C respectively. In each group the animals were of approximately the same age and their weights varied as follows: Group A: 1525 to 1700 grams; Group B: 2120 to 3065 grams, and Group C: 2170 to 2880 grams. Two strains of hemolytic streptococci were used: a strain moderately virulent for rabbits, obtained from one of the patients of the Ear, Nose and Throat Clinic of Billings Hospital and a virulent strain obtained from Dr. Gay. These strains are referred to as strains X and Y respectively.

Vaccines were prepared from strain X, consisting of a 48 hour growth on a blood agar slant, suspended in 2 cc. of a 0.9 per cent salt solution and heated at 60 degrees centigrade for one hour, and with these the animals of Group A were treated. The first four treatments of the animals in Group B were made with vaccines prepared by suspending, in 2 cc. of 0.9 per cent salt solution, a 24 hour growth of the strain Y streptococcus on one blood agar slant, heated at 60 degrees centigrade for one hour. For the next three treatments the vaccines were made in the same way but from the growth on two agar slants and the last from the growth on three slants. Eight treatments in Group C were made

with suspensions of a 36 hour growth on 2, 3, 4, 4, 5, 5, 6 and 8 blood agar slants respectively, prepared as were those for Groups A and B. The treatments were given on alternate days, under ether anesthesia and in doses of 1/20 cc. as follows: 9 animals received injections into each tonsillar region; 8 received one dose placed over each tonsillar region followed by massage; in 3 animals the injections were made into the mucosa of each cheek; 4 received an injection into one tonsillar region and another into the mucosa of one cheek; 2 received injections of 1/20 cc. of 0.9 per cent sterile salt solution into each tonsillar region and 8 animals were used as controls. The massage consisted of 60 to-and-fro strokes with a glass rod over each tonsil.

In Group A only four treatments were given because five of the animals died. Those which survived were allowed to rest for ten days; were then given an injection into each tonsillar area of 1/20 cc. of a suspension of live organisms of strain X, of the same concentration as the vaccines used in their previous treatments, and were killed by air embolism forty-eight hours later. In Groups B and C eight treatments were given; the animals were allowed to rest for three weeks; were then given injections into each tonsillar and cheek region of concentrated suspensions of live streptococci of strain Y in 1/20 cc. doses and were killed by air embolism at intervals ranging from 2 to 72 hours following the final injection. The concentrated suspensions used in Groups B and C consisted of a 36 hour growth of strain Y on veal infusion agar in 3 Kolle flasks, suspended in 3 cc. of sterile distilled water.

The whole soft palate of each animal, in most instances with the roof and sides of the nasopharynx as well, was excised en masse, fixed in formol-Zenker fluid and embedded in celloidin. In Group A sagittal serial sections of the palate were made at 12 microns. In Groups B and C the site of injection into the cheeks was excised, fixed and embedded in the same way. In these groups frontal sections of the palate and sections of the cheek in a horizontal plane were made at from 12 to 15 microns. Every tenth section in each case was mounted serially and stained with Maximow's hematoxylin-eosin-azur II. Wherever the presence of bacteria was indicated in these, additional sections were mounted and on these Gram stains were made according to the method of

Brown and Brenn (25). In order to determine tonsillar size, two diameters were obtained by measurement of the largest section of each tonsil with a vernier caliper and the third was computed by multiplying the thickness of each section in microns times the number of sections made of each tonsil.

DISCUSSION OF PROCEDURES

A hemolytic streptococcus was used because in the majority of the bacteriological studies on the tonsil this organism has been found to be the chief offender in the production of acute tonsillitis in man. The rabbit was used because it was the largest of the small laboratory animals available at the time this study was undertaken. The small size of the rabbit's palatine tonsils made it impossible to limit this study to the tonsils themselves, consequently, the results obtained apply to the whole tonsillar region and not solely to the tonsils.

The treatments in which the vaccines were massaged into the tonsillar region were made because presumably it is in this way that inoculation of the tonsil crypts occurs in man. Injections into only one tonsillar region and into one cheek were made in some instances in order to determine whether the treated tonsillar area would show greater immune response than its fellow, though the animal as a whole received the same amount of vaccine as those in which the injections were made into each tonsillar region. In order to compare the degree of local immunity developed in the tonsillar region with that developed elsewhere in the oral cavity, in some animals the tonsillar region was spared and the vaccination carried out in the cheeks. In making the suspension of virulent organisms for the final injection, veal infusion agar was used instead of blood-agar, which contained sheep's blood and had been used in the preparation of the vaccines, in order to reduce the possibility of having matter, other than the organisms injected, playing a part in the immune reactions produced. Further, the suspension was made in distilled water rather than in 0.9 per cent salt solution because the streptococcus tends to agglutinate spontaneously in normal saline. No effort was made to desensitize the animals in order to destroy or minimize their allergic response to the final streptococcus injection. The reactions produced were measured, therefore, in terms of both the inflammatory response and the degree of locali-

zation of the bacteria.

In order to obtain the largest number of stages possible in the development of the final reaction, the last injections in each animal were not made simultaneously into each side but with an interval of two or more hours. Thus each animal represented two stages in the development of the allergic and immune reactions.

Access to the tonsillar region was gained in the following way: Each rabbit was anesthetized with ether, placed supine on a guinea-pig board and its mouth held open by means of a clamp made for this purpose and attached to an iron stand. The tonsils were then exposed by means of a funnel-shaped speculum made from a Pyrex glass test-tube 16 or 18 mm. in diameter and 150 mm. long. The injections were made with a 1 ml. tuberculin type Luer syringe, through a Yale needle gauge number 24 and $1\frac{1}{2}$ inches long.

RESULTS

Immunity was established only in part in Group A, for which reason the results obtained in this group, though suggestive were not considered in drawing conclusions.

All of the animals treated with vaccines showed enlargement of the tonsils, most marked in those treated by injections into the tonsillar area, whereas in the controls and in those injected with 0.9 per cent salt solution, the tonsils remained small (Table III). This enlargement was in the form of an hyperplasia similar to that observed in hyperplastic human tonsils but differing in that the so-called germinal centers of the follicles were not as distinct.

TABLE III
AVERAGES OF TONSILLAR ENLARGEMENT

Treatment	Number of Animals	Size in cu. mm.
Nothing done.....	8	26.67
Saline injected into tonsils....	2	22.43
Vaccine injected into one tonsil	4	34.68
Vaccine massaged into tonsils...	8	39.02
Vaccine injected into cheeks....	3	43.78
Vaccine injected into tonsils...	9	47.61

The reaction to the final injection of live bacteria varied in the groups receiving the different forms of treatment and in the controls. In grading the findings in each animal, the degrees of reaction were recorded as "none," "slight," "medium" and "marked." In estimating the numerical averages for the whole series these words were represented by the figures "0," "1," "5" and "9" respectively, so that the averages ranged from zero to nine. On the basis of the numbers obtained in this way, the inflammatory response of the tonsillar area to the final injection of live streptococci in the actively immunized animals was not found to be attended by a more marked polymorphonuclear leucocytic infiltration than in the controls, neither was the fibrin response greater nor was there a larger subepithelial collection of mononuclear cells adjacent to the tonsils other than at the site of injection. There was, however, a distinct difference shown by the greater degree of mononuclear response at the site of injection, the better localization and clumping of bacteria and the better localization of the resulting abscess at the inoculated site. These changes were least in the controls and progressively more marked in the animals treated by massage or saline injections, two cheek injections and one cheek and one tonsillar injection. In the two controls used in Group C the infection extended as a clearly visible cellulitis around the pharynx and down its dorsal wall into the neck, whereas in the immunized animals the area of grossly visible infection remained localized to the soft palate. Though there was no appreciable difference in the size of the two tonsils of the four animals receiving injections of vaccines into only one tonsillar area, the immunized side showed a slightly better localization of bacteria and a more pronounced macrophage response than the non-immunized side.

The mononuclear cell response in the immunized animals consisted of lymphocytes, plasma cells and successively larger cells up to those which were clearly macrophages. In several instances lymphatics dilated with lymphocytes could be traced in serial sections from the tonsil to the site of infection where larger cells appeared, suggesting the tonsil as a possible source of the macrophages seen in this response to infection in the actively immunized animals. In many instances the macrophages were arranged as a peripheral zone about an abscess of polymorphonuclear leucocytes, in some of which bacteria could still be seen

and in others about masses of disintegrating cells without definite traces of bacteria. Phagocytosis by microphages was not striking but macrophages phagocytosis of bacteria was marked.

Aside from clumping as an indication of the resistance of the immunized animals, the cocci lost their arrangement in chains and showed marked variations in size and in the degree to which they took the Gram stain as the process became older. Though similar changes appeared in the controls, they were less marked and developed more slowly.

A comparison of the response to immunization of the tonsillar region with that of the mucosa of the cheeks, revealed in these animals that the local immunity produced in the tonsillar region was not significantly greater than that produced in the cheek region.

DISCUSSION

The results of this study agree, in general, with those obtained by Cannon and Pacheco (18). In the immunized animals the final injection of live and virulent bacteria was followed by a prompt inflammatory reaction, rich in macrophages, which was associated with a massing of bacteria, suggestive of an *in vivo* agglutination reaction. Though the macrophage response occurred as early as the second hour, mechanical factors due to a marked cellular infiltration of the tissues at the site of injection, did not appear to play a part in the production of the bacterial clumping which occurred.

The part played by the lymphocyte in acute inflammations is suggested in this study by the cells seen in all stages of transition from lymphocytes to macrophages as well as by the presence of lymphatics dilated with lymphocytes, which were traced in serial sections from the tonsils to the sites of acute inflammation where the transition forms were seen. These findings are in keeping with the idea that the tonsil is an organ of defence as a site of storage of potential macrophages. On the other hand, the very slight differences in immune and allergic response between the tonsil and the cheek regions, fail to support the idea that the tonsil is an effective organ of defence in this way.

CONCLUSIONS

1. Active local immunity to the hemolytic streptococcus can be produced in the region of the palatine tonsil of the rabbit by the local injection of specific vaccines and apparently to a very slight degree by massaging the vaccines into the tonsil.
2. This local immunity is associated with hyperplasia of the palatine tonsil.
3. The tonsillar region does not show a greater immunological response than the subepithelial tissues of the mucosa of the cheek as produced and measured in this study.

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